DEPARTMENT OF HEALTH & HUMAN SERVICES
Food and Drug Administration
New England District

One Montvale Avenue
Stoneham, Massachusetts 02180
TEL 781.596.7700
FAX 781.596.7896

March 8, 2002

WARNING LETTER

NWE -14- 02W

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Mr. L. Dennis Kozlowski
Chairman of the Board & Chief Executive Officer
Tyco International Ltd.
One Tyco Park
Exeter, NH 03833

Dear Mr. Kozlowski:

During an inspection of your establishment located at 22 Terry Avenue, Burlington, MA and 6 Cook Street, Billlerica, MA on October 29 through November 7, 2001, our Investigator determined that your establishment manufactures cerebrospinal fluid (CSF) products, including shunts and catheters. These products are devices as defined by Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

This inspection was conducted to evaluate your compliance with the Medical Device Quality Systems Regulations and to perform a pre-approval inspection [redacted]

This inspection revealed that these CSF devices are adulterated within the meaning of Section 501(h) of the Act, in that the methods used in, or the facilities or controls used for manufacturing, packing, storage, or installation are not in conformance with the Quality System Regulation for medical devices, as specified in Title 21, Code of Federal Regulations (CFR), Part 820 because of the following observations:

1. Failure to document corrective and preventative actions as required by Radionics' Preventive and Corrective Action Procedure SOP QS2-14-0001, Rev. G and CFR 820.100(b). Corrective Action Reports (CARs) cited in the FDA-483 contained numerous documentation deficiencies such as lack of required signatures and missing pages. In addition, many CARs failed to identify:

   a. The cause of the non-conformances;

   b. The action(s) needed to correct and prevent recurrence of nonconforming product and other quality problems;

   c. The action(s) taken to verify or validate the corrective and preventive action and ensure that such action is effective and does not adversely affect the finished device;

   d. The method(s) taken to implement the necessary corrective and preventive actions; and

   e. The action(s) taken to ensure that information related to quality problems or nonconforming product is disseminated to the responsible parties.

2. Failure to establish and maintain procedures for monitoring and control of process parameters for validated processes to ensure that the specified requirements continue to be met as required by 21 CFR 820.75(b). For example, Radionics' Pyrogen Procedure QS3-09-0065, Rev. A does not specify that all implanted device configurations be tested for pyrogenicity; and

3. Failure to validate processes with a high degree of assurance where the results of a process cannot be fully verified by subsequent inspection and test as required by 21 CFR 820.75(a). For example:

   a. The packaging process was last validated in 1994 and not revalidated after changes were made to the sterilization cycle in 1996. Your firm failed to demonstrate adequate documentation that justifies a decision for not revalidating the packaging process after makes these changes; and

   b. The ethylene oxide sterilization process was last validated in 1996 and has not been revalidated annually as required by Radionics' Ethylene Oxide Sterilization Validation Procedure, SPI #11471, Rev. I. In addition, this sterilization process has not been validated since Engineering Change Orders (ECOs) IM1434 and 1250 were implemented in 1998. ECO IM1434 was identified as corrective and preventive action (complaint numbers 2000-467 and 568) and specified changes made to molding parameters and materials. ECO 1250 was identified as a preventive action and specified a dimensional change. The impact of these changes on the effectiveness of the sterilization process can not be adequately assessed without performing a validation. Your firm failed to demonstrate adequate documentation that justifies a decision for not revalidating the sterilization cycle after these changes were implemented.

Furthermore and related to the failure to revalidate the sterilization process, our inspection noted your firm's failure to comply with a commitment stated in the 510(k) notification for the Contour Flex Valve. Specifically, a commitment was made to audit the sterilization cycle annually. As was previously noted, the ethylene oxide sterilization process was last validated in 1996 and has not been revalidated annually. This deficiency is significant and raises concern over the degree of conformance to other commitments stated in 510(k) notifications for all other devices produced by your firm. As a result, we request a thorough review be conducted of all 510(k) notifications that were subsequently approved and an assessment made as to the current level of conformance to all commitments made in such notifications.

In addition, deviations from the Medical Device Reporting Regulations (MDR), Title 21, CFR, Part 803 were observed with your shunt valves and reservoirs. Such deviations render these devices misbranded within the meaning of section 502(t)(2) [U.S.C. 352(t)(2)] of the Act. Specifically, your firm failed to submit information to the FDA as required by the MDR Regulation for:

Complaint Number 2000-568:

This complaint describes an incident with a Radionics Equi-Flow Hydrocephalic Shunt Valve. The complaint stated that the physician observed over drainage in three patients implanted with the device. The Radionics evaluation report confirmed the complaint. A slit in the dome over the siphon limiter was discovered. A leaking device would be likely to cause or contribute to a death or serious injury should the leak recur. Therefore, this incident should be reported in accordance with the provisions set forth in 21 CFR Part 803 as a malfunction.

Complaint Number 2000-467:

This complaint describes an incident with a Radionics Equi-Flow Hydrocephalic Shunt Valve. The complaint indicated that fluid leakage was detected from the outskirts of a siphon valve by the physician before the device was implanted. Radionics examined and retested the device. A slit was found in the bottom of the dome. This incident should be reported in accordance with the provisions of 21 CFR Part 803 as a malfunction.

Complaint Number MP16, RAN 5918:

This complaint describes an incident involving a Contour-Flex Valve Shunt with an integral Rickham Reservoir. The complaint stated that two patients experienced Rickham reservoir fractures after one year of device implantation. A fractured device would be likely to cause or contribute to a leak. A leaking device would be likely to cause or contribute to a death or serious injury should the leak recur. Therefore, this incident should be reported in accordance with the provisions of 21 CFR Part 803 as a malfunction.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and regulations. The specific violations noted in this letter and in the FDA Form 483 issued at the conclusion of the inspection may be symptomatic of serious underlying problems in your establishment's manufacturing and quality assurance systems. You are responsible for investigating and determining the causes of the violations identified by the FDA. If the causes are determined to be systems problems, you must promptly initiate permanent corrective actions.

Federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts. Additionally, no premarket submissions for Class III devices to which the Quality System/GMP deficiencies are reasonably related will be cleared or approved until the violations have been corrected. Also, no requests for Certificates to Foreign Governments will be approved until the violations related to the subject devices have been corrected.

In order to facilitate FDA in making the determination that such corrections have been made and thereby enabling FDA to withdraw its advisory to other federal agencies concerning the award of government contracts, and to resume marketing clearance for class III devices for which a 510(k) premarket notification or Premarket Approval application (PMA) has been submitted, and Certificates to Foreign Governments for products manufactured at your Billerica and Burlington, MA facilities, we are requesting that you submit to this office on the schedule below, certification by an outside expert consultant that he/she has conducted an audit of your establishment's manufacturing and quality assurance systems relative to the requirement of the device Quality System regulations (21 CFR Part 820). You should also submit a copy of the consultant's report and certification by your establishments' CEO (if other than yourself) that he/she has reviewed the consultant's report and that your establishment has initiated or completed all corrections called for in the report. The attached guidance may be helpful in selecting an appropriate consultant.

The initial certifications of audit and corrections and subsequent certifications of updated audits and corrections (if required) should be submitted to this office by the following dates:

Initial certifications by consultant and establishment – June 2002; and

Subsequent certifications – December 2002 and December 2003.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action being initiated by the Food and Drug Administration without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil penalties.

We acknowledge receipt of written correspondence from Michael P. Collette dated November 29, 2001 that was provided in response to the FDA-483's left at your establishments in Burlington and Billerica, MA. The response to FDA-483 Observation 1 made at your Billerica facility is not adequate. This response stated Radionics' personnel conducted periodic reviews of

the sterilization loads and concluded that, since no significant changes took place on products or their designs, revalidation was not necessary. We question the validity of this response as no documentation was made available during our inspection that would substantiate periodic reviews were actually conducted. In addition, design changes were implemented in 1998 as described in ECOs IM1434 and 1250 and previously discussed in this letter. As a result, we question the appropriateness of continuing to ship product for which you lack sterility assurance.

We have a similar concern about continuing to ship product whose packaging integrity is questionable. This concern is magnified knowing: (1) your sterilization cycle has changed since the last time packaging integrity was validated in 1994; and (2) you have received at least one complaint (No. 9000470 resulting in Deviation No. 101) associated with a packaging related problem.

Please notify this office in writing within 15 working days of receipt of this letter of the specific steps you have taken to comply with our request and correct the noted violations. Include an explanation of each step being taken to identify and correct any underlying system problems necessary to assure that similar violations will not recur. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed. We will not schedule an inspection to verify correction of the noted violations until we have received your written certification. Failure to confirm in writing that corrections have been made may result in continued withholding of your approval for PMA P82001/S7.

Your response should be sent to James A. DiNovo, Compliance Officer, Food and Drug Administration, One Montvale Avenue, Stoneham, MA 02180. You may call Mr. DiNovo at **781-596-7720** with any questions regarding this Warning Letter.

Sincerely yours,

Gail T. Costello
District Director
New England District

Enclosure: Selecting a Consultant

Cc:

Mr. Kevin Gould
Pres. of Tyco Healthcare, North America
The Kendall Co.
15 Hampshire Street
Mansfield, MA 02048

Mr. Rick Granger
President of Valleylab
Radionics, Inc.
5920 Longbow Drive
Boulder, CO 80301

Mr. Stephen Hanlon
Vice President
Radionics, Inc.
22 Terry Avenue
Burlington, MA 01803